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10/613,018	07/07/2003	Ursula-Henrike Wienhues	2923-543	8627

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
02/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/613,018	WIENHUES ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2007 and 20 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-22* is/are pending in the application.

4a) Of the above claim(s) *5,8,13 and 15-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,7,9-12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/776,188.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The amendment to the claims received on September 6, 2006 canceled claim 2 and amended claim 1.

The amendment to the claims received on April 25, 2007 canceled claims 23-24 and amended claim 1.

The amendment to the claims received on November 19, 2007 amended claims 1 and 16.

Claims 1 and 3-22 are currently pending.

Claims 1, 3-4, 6-7, 9-12, and 14 are currently under consideration.

Election/Restrictions

2. This application contains claims 16-18 drawn to an invention nonelected without traverse in the reply filed on February 10, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

3. The present application claims status as a DIV of 08/776,188 filed January 24, 1997 (now U.S. Patent 6,613,530) which is a national stage (i.e. 371) of PCT/EP95/02919 filed July 24, 1995. In addition, the present applications claims foreign priority to German applications P 44 26 276.0 filed July 25, 1994 and P 44 30 972.4 filed August 31, 1994.

Invention as Claimed

4. A method for detection of an antibody against a pathogenic organism in a liquid sample wherein said pathogenic organism is selected from the group consisting of bacteria, viruses, and

protozoa, the method comprising: (a) incubating the following: (1) sample, (2) a solid phase, (3) a first antigen for said antibody wherein the first antigen comprises at least one marker group and comprises multiple epitope regions, said epitope regions being identical in amino acid sequence, and (4) a second antigen for said antibody wherein the second antigen binds to the solid phase under conditions to obtain a complex comprising a solid phase-bound second antigen to which is bound the antibody and to which is bound the first antigen and (b) detecting said antibody by direct or indirect detection of the complex on said solid phase wherein at least said first antigen is of formula $(P\text{-})_nT(\text{-}L)_n$ (i.e. Ia) or $T(\text{-}P\text{-}L_m)_n$ (i.e. Ib) wherein T is a carrier, P is a peptide comprising an epitope region wherein said epitope region is reactive with the antibody, L is the marker group in said first antigen or a group which binds to the solid phase in said second antigen, - is a covalent coupling, n is 2-40, and m is 1-10 and variations thereof.

Claim Objection

5. Claims 1, 3-4, 6-7, 9-12, and 14 are objected to because of the following informalities: claim 1, line 3 of method step b reads "wherein at least said first antigen is of formula (Ia) or (Ib). However, "L" of formula (Ia) or (Ib) then defined as "the marker group in said first antigen or a group which binds to the solid phase in said second antigen". Therefore, if "L" is a group which binds to the solid phase in said second antigen, then the first antigen is not defined by either formula (Ia) or (Ib). The phrase "wherein the first antigen and/or the second antigen is of formula (Ia) or (Ib)" is suggested. Appropriate correction is required.

Withdrawn Rejections

6. The rejection of claims 1, 3-4, 6-7, 9-12, and 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention regarding the transitional phrase "has" and the structure of the first antigen is withdrawn in view of the claim amendments received on November 19, 2007.

7. The rejection of claims 1, 3-4, 6-7, 9-12, and 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention regarding the marker group and complex is withdrawn in view of the claim amendments received on November 19, 2007.

8. The rejection of claims 1, 3-4, 6-7, 9-12, and 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention regarding the second antigen and the solid phase is withdrawn in view of the claim amendments received on November 19, 2007.

9. The rejection of claims 1, 3-4, 6-7, 9-12, and 14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 (particularly claims 24-29) of U.S. Patent No. 5,804,371 is withdrawn in view of the terminal disclaimer filed on December 20, 2007.

Maintained Rejections

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

11. Claims 1, 3-4, 6, 9, 12, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Flavell et al. U.S. Patent 5,618,533 filed December 10, 1993.

For present claim 1, Flavell et al. teach double antigen sandwich assays for detection of *B. burgdorferi* (i.e. bacteria) antibodies comprising (1) incubating patient sera (i.e. liquid sample), solid phase, antigen bound to support (i.e. second antigen), and a labeled antigen (i.e. first antigen with marker) wherein the antigens can be multimeric (i.e. multiple epitopes) and coupled to a carrier and (2) detecting antigen and antibody binding in the bound state on the solid phase (please refer to the entire specification particularly abstract; columns 3-6 and 9-10).

For present claims 3-4, Flavell et al. teach antigens that are part of larger multimeric proteins comprising multiple copies of antigens and/or fusion proteins with repeated sequences of the same block of amino acids (i.e. multiple epitopes; please refer to the entire specification particularly column 5).

For present claim 6, Flavell et al. teach antigens that are part of larger multimeric proteins comprising multiple copies of antigens and/or fusion proteins with repeated sequences of the same block of amino acids (i.e. hapten coupled to antigen), flagellin antigens coupled to other *B. burgdorferi* antigens including OspA and OspB (i.e. haptens), coupled to carriers, and labeled anti-IgG or anti-IgM (i.e. binding partner labeled with a signal generating group) wherein the label can be detected (please refer to the entire specification particularly columns 5-6 and 9-10).

For present claim 9, Flavell et al. teach carriers (please refer to the entire specification particularly columns 6, 9).

For present claim 12, Flavell et al. teach recombinant antigens 35-46 amino acids in length (please refer to the entire specification particularly Figures 2, 4A, 4B; column 5; sequence listing).

For present claim 14, Flavell et al. teach recombinant antigens of 35+ amino acids in length which can be multimers (i.e. multiple epitopes; please refer to the entire specification particularly Figures 2, 4A, 4B; column 5; sequence listing).

Therefore, the presently claimed invention is anticipated by the teachings of Flavell et al.

Arguments and Response

12. Applicants' arguments directed to the rejection under 35 USC 102 (e) as being anticipated by Flavell et al. U.S. Patent 5,618,533 for claims 1, 3-4, 6, 9, 12, and 14 were considered but are not persuasive for the following reasons.

Applicants contend that Flavell et al. does not teach "first and second antibodies both hav[ing] 2 or more peptides covalently bound to a carrier where the epitope regions of the peptides are identical in amino acid sequence and both the first antigen and the second antigen include at least one marker group". In addition, applicants point out that Flavell et al. teach (column 6, lines 21-23) that "larger flagellin polypeptides may be more sensitive, additional flagellin sequences may result in a decrease in specificity".

Applicants' arguments are not convincing since the teachings of Flavell et al. anticipate the method of the instant claims. Flavell et al. teach double antigen sandwich assays which utilize flagellin polypeptides or neuroborreliosis-associated antigens that may be part of a larger multimeric protein comprising multiple copies of flagellin polypeptides or neuroborreliosis-associated antigen (i.e. multiple epitopes), addition of carriers to one or both terminals of the

antigens, and labeled antigens (i.e. marker; please refer to the entire specification particularly column 5, lines 55-67; column 6, lines 1-17; columns 9-10). Regarding column 6, lines 21-23 of Flavell et al., Flavell et al. goes on to suggest ways in which the polypeptides could be altered to offset any decrease in specificity while maintaining high sensitivity (see column 6, lines 18-36; routine optimization by one of skill in the art).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. first and second antibodies; 2 or more peptides bound to a carrier; first and second antigens both include markers) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Please note: it is believed that the recitation of "first and second antibodies" was a typographical error (i.e. first and second antigens with multiple epitopes; taught by Flavell et al., see above). In addition, it is noted that the marker of the present claims is not required to be a peptide, thus the formulas as claimed do not require two peptides to be attached to the carrier except for the chain of 2-10 peptides (i.e. multimeric peptides) bound the carrier (i.e. only one peptide is actually bound to the carrier; other peptides of chain are bound to peptides).

Claim Rejections - 35 USC § 103

13. Claims 1, 3-4, 6-7, 9-12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rejman et al. EP 0 507 586 (supplied by applicants in IDS), Formoso et al. WO 90/07119 published June 28, 1990, and Watts et al. U.S. Patent 5,437,983 filed February 1, 1993.

For present claim 1, Rejman et al. teach immunoassay methods for detecting antibodies comprising (1) incubating a sample, a support, an antigen-small molecule conjugate (i.e. second antigen), and an antigen-signal generating means conjugate (i.e. first antigen with a marker; labeled antigen) wherein the support has a receptor for the small molecule (i.e. second antigen bound to support) and the labeled antigen can also have a small molecule and/or receptor (i.e. carrier) and (2) detection of the signal on the support (please refer to the entire specification particularly abstract; pages 2-4, 7). In addition, Rejman et al. teach that antigens can have multiple determinant sites and typically 2-20 small molecules bound to the antigens (please refer to page 7, lines 46-55).

For present claims 3-4, Rejman et al. teach that the first and second antigens can be the same (please refer to the entire specification particularly page 3).

For present claims 6-7, Rejman et al. teach direct and indirect labeling and detection of the bound antigen (please refer to the entire specification particularly pages 4-5).

For present claims 9-11, Rejman et al. teach small molecules/receptors (i.e. carrier) bound to antigens wherein the carrier can be antibody, Fab, polypeptide (please refer to the entire specification particularly pages 3-4).

However, Rejman et al. does not specifically teach multimers or the size of the antigens.

For present claims 3-4, Formoso et al. teach multimers and polymers of various peptides (e.g. antigens, epitopes, multiple epitope regions of identical amino acid sequence; please refer to entire specification particularly claims 2-9 and 11-18).

For present claims 12 and 14, Formoso et al. teach synthetic peptides conjugated through the C-terminus to a carrier protein which are typically about 5 to about 22 amino acids in length

and preferably 11-20 amino acids or 15-17 amino acids in length (e.g. sequences of 6 to 50 amino acids; please refer to page 3, lines 22-32, page 4, lines 33-35, page 9, lines 24-36).

In addition, the elected species of SEQ ID No: 5 is taught by Formoso et al. including peptides of HIV-1 gp41 with the amino acid sequence of 1-15 of present SEQ ID NO: 5 (please refer to claims 2 and 11). Furthermore, Formoso et al. teach that the carrier protein is preferably BSA, the peptides can be utilized in determining the presence of HIV-1 or HIV-2 antibodies in fluid samples, and that multiple peptides can be utilized in the ELISA, EIA, or RIA assays to determine the presence of HIV antibodies (please refer to pages 3-4 Summary of the Invention section and pages 8-17 Description of the Specific Embodiments section).

However, neither Rajman et al. nor Formoso et al. teach cardiotonic glycoside haptens and indirect detection via antibodies that bind the haptens.

For present claims 6-7, Watts et al. teach digoxigenin (e.g. cardiotonic glycosides) and antidigoxigenin antibody in binding assays with analytes and sbp or specific binding pairs and detecting signals (please refer to column 2, lines 1-18; column 3, lines 3-52; column 4, lines 15-35; column 5, lines 1-4; and Examples).

In addition, Watts et al. teach binding of sbps including antigens to labels to produce a signal producing system, utilizing beads as solid supports, performing the assay in a liquid medium, utilizing BSA, and screening for HIV related antibodies (please refer to column 4, lines 15-29; column 6, lines 41-67; column 7, lines 1-25, column 8, lines 9-51; column 9, lines 3-41; column 10, lines 22-31; column 11, lines 11-63).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detection of viral antibodies taught by Rejman et

al. with the shorter synthetic peptides in multimeric form taught by Formoso et al. and the digoxigenin and anti-digoxigenin detection system taught by Watts et al.

One having ordinary skill in the art would have been motivated to do this because Formoso et al. teach that synthetic peptides allow standardized antigen production, avoidance of nonspecificity resulting from contaminating proteins of *E. coli*, and reduced time of incorporating new antigens necessitated by mutation of HIV peptides which will improve tests for HIV specific antibodies (please refer to page 3, lines 7-20 of Formoso et al.) and Watts et al. teach that various detection and labeling systems can be utilized including enzymatic, radioactive, and fluorimetric wherein one type of detection and labeling systems use is the digoxigenin and anti-digoxigenin detection system (please refer to column 1, lines 21-28).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method for detection of viral antibodies taught by Rejman et al. with the shorter synthetic peptides in multimeric form taught by Formoso et al. and the digoxigenin and anti-digoxigenin detection system taught by Watts et al. because Formoso et al. have shown the success of the screening and identification of antibodies using optimally immunoreactive peptides (please refer to page 11, lines 19-36 and page 12, lines 1-6 and Examples 1-20) and Watts et al. have shown the success of using the detection and labeling systems of digoxigenin and anti-digoxigenin detection system (col. 17, lines 17-47).

Therefore, the modification of the method for detection of viral antibodies taught by Rejman et al. with the shorter synthetic peptides in multimeric form taught by Formoso et al. and the digoxigenin and anti-digoxigenin detection system taught by Watts et al. render the instant claims *prima facie* obvious.

Arguments and Response

14. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Rejman et al. EP 0 507 586 (supplied by applicants in IDS), Formoso et al. WO 90/07119 published June 28, 1990, and Watts et al. U.S. Patent 5,437,983 filed February 1, 1993 for claims 1, 3-4, 6-7, 9-12, and 14 were considered but are not persuasive for the following reasons.

Applicants contend that Rejman et al. does not teach antigens of formulas (Ia) or (Ib) or the use of multimeric antigens with marker groups in double-antigen bridge tests. Applicants also contend that Formoso et al. does not teach antigens with multiple identical epitopes. In addition, applicants contend that Watts et al. does not cure the above alleged deficiencies.

Applicants' arguments are not convincing since the teachings of Rejman et al., Formoso et al., and Watts et al. render the method of the instant claims *prima facie* obvious. Rejman et al. teach immunoassays utilizing a support and two antigens wherein one antigen is bound to a small molecule (i.e. carrier, marker) and another antigen is labeled (i.e. marker, carrier), one antigen is bound to a support, and the labeled antigen can also have a small molecule and/or receptor (i.e. carrier; please refer to pages 3 and 7-9). In addition, Rejman et al. teach that antigens can have multiple determinant sites and typically 2-20 small molecules bound to the antigens (i.e. multiple carriers, multiple markers; please refer to page 7, lines 46-55). Formoso et al. teach multimers and polymers (i.e. repeating structural units; multiple epitopes of the same sequence) of antigens including at least two peptides conjugated to carrier (please refer to claims 2-3, 11, 18).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ADS
January 25, 2008

/Jon D. Epperson/
Primary Examiner, AU 1639